REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 93, 95, and 98-120 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The specification at page 10 is objected to for informalities. Appropriate correction is made, as helpfully suggested by the examiner, thereby obviating this objection.

Claims 93, 95 and 98-119 have been rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The examiner states that the term "mainly" in claim 93 is a relative term which renders the claim indefinite. Claim 118 is rejected on the same grounds.

The phrase "mainly shows a single protein band with an activity of inducing interferon-gamma production" is now amended to instead recite "has an activity of inducing interferon-gamma production". Applicants believe that claims 93 and 118, and claims dependent therefrom are no longer indefinite.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 93, 95 and 98-120 have been rejected under 35 U.S.C. 103 (a) as being unpatentable over Nakamura et al., *Infect. Immun.* 61:64-70 (1993). Despite applicants' arguments, the examiner still maintains this rejections, stating that Okamura's later publication

demonstrated the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver, and further that Okamura discloses "thus IGIF in the serum sample was proved to be the same IGIF as that found in liver extract". This rejection is, however, respectfully traversed.

Okamura states at page 3969, the second paragraph of the left column as follows:

> Thus IGIF in the serum sample was proved to be the same IGIF as that found in liver extract, and it was considered to be bound to another protein or to exist in an oligomeric form.

This statement means that it is not Nakamura but Okamura who first succeeded in purifying and isolating IGF (molecular weight of 19 kDa on SDS-PAGE), which had been neither purified nor isolated by Nakamura. This is supported by the following statements in Okamura's publication;

i) The title of Okamura's publication reads as follows:

"A Novel Costimulatory Factor for Gamma Interferon Induction Found in the Livers of Mice Causes Endotoxic Shock" (emphasis added). This would not be considered "novel" if Nakamura's earlier factor is the same as Okamura's.

ii) Okamura states at page 3972, top of second paragraph in the left column:

"In summary, a novel consimulatory factor (IGIF) for IFN-gamma production cells was isolated from bacterium-treated mice subsequently challenged by LPS." (emphasis added)

Based on these statements, it should be clear that Okamura recognized that he succeeded in newly purifying and isolating IGIF (molecular weight of 19 kDa on SDS-PAGE). If Okamura did not believe that he had found a new substance, then Okamura would not have submitted his paper at the "American Society for Microbiology", which is the oldest and largest single life science membership organization in the world.

Furthermore, with regard to Okamura's statement at page 3969, second paragraph of the left column cited by the examiner, this statement should be considered to be Okamura's speculation about the reasons why Okamura's IGIF is different from the Nakamura's factor in the molecular weight. That is to say, Okamura speculated as follows:

i) "another protein" may have bound to IGIF (molecular weight of 19 kDa on SDS-PAGE) to form Nakamura's partially purified and isolated proteineous factor (molecular weight 75-80 kDa on gel filtration), or

ii) a plurality of IGIF (molecular weight of 19 kDa on SDS-PAGE), newly purified and isolated by Okamura, existed in oligomeric form to be isolated as Nakamura's partially purified and isolated proteineous factor (molecular weight 75-80 kDa on gel filtration).

It should however be noted that Okamura never confirmed if any of the above speculations were true. Applicants submit that Okamura never states that his IGIF is the same substance as Nakamura's factor.

In connection with this prior art issue, a Schematic Diagram showing the differences between IGIF and Nakamura's factor is attached hereto for the examiner's consideration. The Schematic Diagram was

prepared by the applicants on the basis of Nakamura's and Okamura's publications. As is evident from the Schematic Diagram, it would be unreasonable for one of ordinary skill in the art to consider Nakamura's factor to be same as the presently recited IGIF.

Furthermore, as applicants pointed out in the arguments of the amendment filed February 22, 2007, "The Cytokine Handbook" second edition, edited by Angus W. Thomson, pp.23-224, 1994, states as follows:

> Monoclonal antibodies specific for mouse IL-10 revealed that, as for many other cytokines, some IL-10 molecules appear to be nonfunctional and antigenically different, since two monoclonal antibodies were isolated that bound IL-10 but did not recognize any biologically active molecules (Mosmann et al., 1990).

This implies that the molecular species of 19 kDa derived from Nakamura's factor may be different from the IGIF or IL-18 of the claimed invention in its antigenicity. In view of this, it is considered that the molecular species of 19 kDa derived from Nakamura's factor may not have been effective to obtain a monoclonal antibody which recognizes IGIF or IL-18.

In addition, both Nakamura and Okamura do not recite that they actually obtained monoclonal antibodies which recognize IGIF even though they did indicate the necessity of such monoclonal antibodies.

Accordingly, Nakamura's factor does not make obvious the presently claimed invention.

Reconsideration and withdrawal of this rejection are respectfully solicited.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early consideration and early allowance are earnestly urged.

Respectfully submitted,

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